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New fluoroazetidinone derivs. - useful as intermediates for fluorocarbapenem antibiotics

Patent Assignee: SAGAMI CHEM RES CENTRE (SAGA)
Number of Countries: 001 Number of Patents: 001
Abstract (Basic): JP 63017859 A

New fluoroazetidinone derivs. are of formula (I). In (I) R1 is H or trialkylsilyl; R2 is H or amino-protecting gp.

The reaction is carried out in presence of an imidazole (e.g. imidazole at a temp. of -78 to 100 deg.C. Redn. of (IV) is achieved with L-selecdride, zinc borohydride, NaBH4, diisobutyl-aluminium 2,6-di-t-butyl-4-methylphenoxide, etc. in a solvent chosen from THF, Et2O, MeOH, EtOH, benzene, toluene, xylene, etc. according to the reducing agent used. The reaction proceeds smoothly at -80 deg.C or room temp. Fluorination of (V) is achieved with diethylaminofluorochloroethane, phenyltetrafluoro-phosphorane, difluorotriphenylphosphorane, diethylaminosulphur trifluoride, piperidinosulphur trifluoride, perfluoropropene-dialkylamine, etc. The reaction is conducted in a solvent, e.g. CH2C12, CHC13, Et2O, THF, at a temp. of -110 - 100 deg.C, pref. -11=-25 deg.C.

USE/ADVANTAGE - (I) is useful as intermediate in prepn. of fluorocarbapenem antibiotics. (I) may be prepd. from diketene (II) and cpd. (III).

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Title Terms: NEW; FLUORO; AZETIDINONE; DERIVATIVE; USEFUL; INTERMEDIATE; FLUORO; CARBA; PENEM; ANTIBIOTIC
Derwent Class: B03
International Patent Class (Additional): C07D-205/08

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WPI Acc No: 1992-363097/199244
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New fluorine-contg. azetidinone derivs. - useful as intermediates to antibacterial fluorine-contg. carbapenem derivs.

Patent Assignee: DAIICHI PHARM CO LTD (DAUC)
Number of Countries: 001 Number of Patents: 001

Abstract (Basic): JP 4266869 A

F-contg. azetidinone derivs. of formula (I) (where R1 is H, OH-protecting groups; R2 is H, lower alkyl; R3 is H, COOH-protecting gps.) are new.

USE/ADVANTAGE - The F-contg. prods. obtd. are useful as synthetic intermediates to carbapenem derivs. whose carbapenem skeleton possesses a side chain substd. with a F atom at 4 position of the skeleton. The F-contg. carbapenem derivs. have excellent antibacterial properties.

In an example, a mixt. of 22mg (3S,4S)-3-(1'R)-1'-(tert.-butyldimethyl silyloxy)ethyl) -4-(1''-ethoxycarbonyl-1''-fluoro-2''-hydroxyethyl) azetidin-2-one and 32mg Ph3P in 2 ml CCl4 was refluxed for 16 hrs. The reaction mixt. was diluted with Et2O and worked up to give, from the organic layer, 191mg (3S,4S)3-3((1'R)-1'-(tert.-butyldimethyl silyloxy)ethyl -4(2''-chloro-1''-ethoxycarbonyl-1''- fluoroethyl) azetidin-2-one (II). To a mixt. of 17mg (II) and 3mg 2,2'-azobisisobutyronitrile in 1ml anhydrous, C6H6 was added 0.1ml n-Bu3SnH in 1ml anhydrous C6H6 under reflux. Reflux was contained for 16 hrs. 1ml CCl4 was added, followed by reflux for another hr. To the reaction mixt. were added 10% aq. NH3 and then Et2O. The organic layer was washed with H2O and concd. The residue was chromatographed on SiO2 gel in 5:1 hexane-EtOAc to elute 12.6mg (3S,4S)-3-((1'R)-1'-(tert.-butyldimethylsilyloxy)ethyl)) -4-1''-ethoxycarbonyl-1''-fluoroethyl) azetidin-2-one.

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Title Terms: NEW; FLUORINE; CONTAIN; AZETIDINONE; DERIVATIVE; USEFUL; INTERMEDIATE; ANTIBACTERIAL; FLUORINE; CONTAIN; CARBA; PENEM; DERIVATIVE
Derwent Class: B03
International Patent Class (Main): C07D-205/08